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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,149	11/17/2003	Robert H. Getzenberg	076333-0331	9439

7590 03/06/2008

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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
03/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,149	GETZENBERG, ROBERT H.	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *2-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/20/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed December 19, 2007 in response to the Office Action of July 20, 2007 is acknowledged and has been entered. Claims 1 and 17-21 have been amended.

2. Claims 1 and 17-24 are currently being examined.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 1 remains rejected and claims 17-24 are rejected under 35 USC 112 1st para. as lacking an adequate written description for the reasons previously set forth in the Office Action of 7/20/2007, section 6, pages 4-7.

Applicants argue that although not acquiescing to the merits of the Examiner's rejection, Applicant has deleted "about" from claims 1 and 17-24, as noted above. Applicant submits that the claims satisfy the written description requirement, and he requests withdrawal of the rejection.

Applicant's arguments have not been found persuasive because, although "about" has been deleted, as previously set forth, Applicants have stated on the record, that molecular weights and isoelectric points can vary slightly depending on particular test conditions.

Additionally Applicants state on the record in regard to the Rule 132 declaration on page 1 of the remarks

> More specifically, Dr. Getzenberg underscores a common understanding in the art, namely, that molecular-weights and isoelectric-points can vary slightly for a particular protein. As he attests in paragraph 6, these variations are caused by many factors, including post-translational changes in proteins and test conditions of two-dimensional

> electrophoresis, whereby proteins can be separated by their molecular-weight and isoelectric-point.
>
> Accordingly, a given protein from different sources can be presented with slightly different molecular weights and isoelectric points. As Dr. Getzenberg also attests, those skilled in the field can recognize when such variation is slight or significant, which enables the field to identify proteins with reasonable precision, notwithstanding the aforementioned variations in molecular-weights and isoelectric-points. By the same token, even without the recitation of "about," as mentioned above, claims 1 and 17-24 accommodate slight variations in the molecular-weights and isoelectric-points recited.

Given the stated variation in molecular and isoelectric points encountered in two-dimensional electrophoresis which depend on several different variables, the claims encompass proteins, and antibodies to said proteins, which do not have the same MW and pI of those isolated by Applicants. Thus, it is clear that one of skill in the art cannot readily visualize or recognize the identity of members of the genus to which the antibodies are directed. Although proteins in two-dimensional electrophoresis gels can be recognized with reasonable precision, given the variability in performing said gels, the claims and specification provide insufficient information to recognize the genus of protein to which the antibodies are directed.

The Declaration under 37 CFR 1.132 filed 12/19/20007 is insufficient to overcome the rejection of claims 1 and 17-24 under 35 USC 112 1st para. as lacking an adequate written description for the reason set forth above and in the Office Action of 7/20/2007, section 6, pages 4-7.

Applicant's arguments have not been found persuasive and the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Konety et al. (Journal of Urology, March 27, 1997, 157:278 Abstract 1074, IDS, see Appendix 1 for date), in view Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 141-142), and in further view of Sambrook et al. (Molecular Cloning: A Laboratory Manual, 1989, p. 18.70- 18.75).

The claims are drawn to monoclonal, polyclonal and detectably labeled antibodies directed against a nuclear matrix protein or an immunogenic fragment thereof in a human subject, wherein said protein is absent in normal renal cells but present in cancerous renal cells

and is selected from the group consisting of: (a) RCCA-1 having a molecular weight of about 53 kD and a pI of about 9.30; (b) RCCA-2 having a molecular weight of about 32 kD and a pI of about 6.95; (c) RCCA-3 having a molecular weight of about 27 kD and a pI of about 6.50; (d) RCCA-4 having a molecular weight of about 20 kD and a pI of about 5.25; and (e) RCCA-5 having a molecular weight of about 15 kD and a pI of about 6.00.

Konety et al. teach extracting and analyzing nuclear matrix proteins from 15 renal cell carcinoma patients using two dimensional electrophoresis. Konety et al. teach identifying five characteristic and unique nuclear matrix proteins that were found in all 15 samples of renal cell carcinoma that were absent in the normal renal tissue. Konety et al. teach that the there was no significant variation in the protein composition of histologic types of RCC. Konety et al. teach that all of the nuclear matrix proteins analyzed were present in the cell lines A-498 and 769-P. Konety et al. teach that of the 15 renal cell carcinoma patients analyzed, 10 patients had clear cell histology, 1 had granular pattern, 2 had mixed granular and clear cell, 1 had sarcomatoid and clear cell patterns, and 1 was a poorly differentiated tumor.

Although the reference does not specifically state that the proteins were a) RCCA-1 having a molecular weight of about 53 kD and a pI of about 9.30; (b) RCCA-2 having a molecular weight of about 32 kD and a pI of about 6.95; (c) RCCA-3 having a molecular weight of about 27 kD and a pI of about 6.50; (d) RCCA-4 having a molecular weight of about 20 kD and a pI of about 5.25; and (e) RCCA-5 having a molecular weight of about 15 kD and a pI of about 6.00, given that that the inventor is a co-author of the prior art, given that the patient population is nearly identical to that used in the instant specification (see Table 1), given that the instantly claimed proteins and the proteins of the prior art are present in the cell lines A-498

and 769-P (see page 23, lines 23-24, and page 26, lines 12-18), the claimed proteins appear to be the same as the prior art proteins, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Harlow and Lane teach that the usefulness of monoclonal antibodies stems from three characteristics- their specificity of binding, their homogeneity, and their ability to be produced in unlimited quantities. The production of monoclonal antibodies allows the isolation of reagents with a unique, chosen specificity. Harlow and Lane teach that because all of the antibodies produced by descendants of one hybridoma cell are identical, monoclonal antibodies are powerful reagents for testing for the presence of a desired epitope. Harlow and Lane teach that hybridoma cell lines also provide an unlimited supply of antibodies, see p.141.

Harlow and Lane teach that, although in theory monoclonal antibodies can be used for all of the tasks for which polyclonal antibodies are used, polyclonal antibodies are easier to produce and may be better for specific techniques, see p. 142, first para., and Table 6.1.

Sambrook et al. teach detectably labeling antibodies for immunological detection of proteins by western blots, see p. 18.70-18.75.

It would have been *prima facie* obvious to one of ordinary skill in the art to have produced antibodies to the renal cell carcinoma protein antigens isolated by two dimensional gel

electrophoresis of Konety et al because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. See Ex parte Ehrlich, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1987), Ex parte Sugimoto, 14 USPQ 2d 1312 (PTO Bd. Pat. App. & Int. 1990). Additionally because of their expression in renal cell carcinomas and not in normal kidney tissues one of skill in the art would have been motivated to make antibodies to the proteins of Kontey et al. because of the importance of understanding the functions of proteins involved in renal cell tumorigenesis to design better treatments for this disease.

Given that the prior art reference is co-authored by the inventor of the instant application, given that the proteins are isolated from the same source as that taught in the prior art publication, one would have a reasonable expectation of success in producing antibodies that bind to the claimed proteins.

Further, it would have been prima facie obvious and one of ordinary skill in the art would have been motivated to make monoclonal antibodies because Harlow and Lane teach the advantages of having an unlimited supply of homogeneous antibodies that have a defined specificity. Additionally, one would have been motivated to produce polyclonal antibodies to the proteins of Kontey et al. because Harlow and Lane teach that polyclonal antibodies are easier to produce than monoclonal antibodies and may be more useful for specific immunological techniques. Given the conventional nature of the production of monoclonal and polyclonal antibodies at the time the invention was made, one would have had a reasonable expectation of successfully producing monoclonal and polyclonal antibodies the proteins of Kontey et al.

Further, it would have been prima facie obvious and one would have been motivated to label the antibodies for use in the well known art method of western to detect the proteins of Kontey et al. using antibodies that are directly or indirectly labeled with a secondary antibody or other reagent, see Sambrook et al. p. 1870-1875.

Thus, one of skill in the art would be motivated with a reasonable expectation of success to make labeled monoclonal or polyclonal antibodies to the proteins of claim 1.

6. All other objections and rejections recited in the Office Action of July 20, 2007 are withdrawn.

7. No claims allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Peter J Reddig/

Examiner, Art Unit 1642

/P. J. R./

/Karen A Canella/

Primary Examiner, Art Unit 1643